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Dated 21 August 2003

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F01[redacted]00 0.00-0217973.7

1/77

# Request for grant of a patent

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Cardiff Road
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1. Your reference

NO2/0321/GB

2. Patent application number
*(The Patent Office will fill in this part)*

0217973.7

3. Full name, address and postcode of the or of each applicant *(underline all surnames)*

Rudy Hengelmolen

c/o Ralinea Limited
The Heath Business & Technical Park
Runcorn
Cheshire WA7 4QF

Patents ADP number *(if you know it)*

If the applicant is a corporate body, give the country/state of its incorporation

8438590001

4. Title of the invention

DUCT LINERS

5. Name of your agent *(if you have one)*

McNeight & Lawrence

"Address for service" in the United Kingdom to which all correspondence should be sent *(including the postcode)*

Regent House
Heaton Lane
Stockport
Cheshire
SK4 1BS

Patents ADP number *(if you know it)*

0001115001

6. If you are declaring priority from one or more earlier patent applications, give the country and the date of filing of the or of each of these earlier applications and *(if you know it)* the or each application number

| Country | Priority application number *(if you know it)* | Date of filing *(day / month / year)* |
|---|---|---|
| | | |

7. If this application is divided or otherwise derived from an earlier UK application, give the number and the filing date of the earlier application

| Number of earlier application | Date of filing *(day / month / year)* |
|---|---|
| | |

8. Is a statement of inventorship and of right to grant of a patent required in support of this request? *(Answer 'Yes' if:*

*a) any applicant named in part 3 is not an inventor, or*
*b) there is an inventor who is not named as an applicant, or*
*c) any named applicant is a corporate body.*
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No

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| | |
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| Continuation sheets of this form | |
| Description | 12 |
| Claim(s) | |
| Abstract | |
| Drawing(s) | 6 |

10. If you are also filing any of the following, state how many against each item.

| | |
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| Priority documents | |
| Translations of priority documents | |
| Statement of inventorship and right to grant of a patent *(Patents Form 7/77)* | |
| Request for preliminary examination and search *(Patents Form 9/77)* | |
| Request for substantive examination *(Patents Form 10/77)* | |
| Any other documents *(please specify)* | |

11. I/We request the grant of a patent on the basis of this application.

Signature: McNeight & Lawrence — Date: 1 August 2002

12. Name and daytime telephone number of person to contact in the United Kingdom: A R Collingwood 0161 480 6394

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# DUCT LINERS

This invention in its broader aspects relates to components for use in lining ducts. One specific application of the invention is concerned with stents for use in counteracting obstructions or narrowing in *in vivo* ducts such as blood vessels, bile ducts in the liver or pancreas, gastrointestinal tubes such as the esophagus, urethra and ureter ducts and pulmonary passageways.

According to the present invention there is provided a tubular liner for insertion into a duct, the liner being open at both ends so as to allow fluid flow therethrough, characterised in that the liner comprises an auxetic material.

References to auxetic material herein include materials which are intrinsically auxetic and materials which have been rendered auxetic (as discussed hereinafter).

Conventional materials have a positive Poisson ratio, i.e. when stretched in one direction they tend to become thinner in a direction lateral to the direction of elongation. Auxetic materials exhibit a negative Poisson ratio in that they expand in a direction perpendicular to the direction of stretching. Auxetic materials also have the capacity for formation into doubly curved or dome shaped surfaces due to the synclastic property of auxetic materials, a property which is described in for instance International Patent Application No. WO 99/22838 with reference to Figure 2(b) thereof.

The auxetic material may be a synthetic auxetic material and may have a macroscopic or microscopic auxetic structure.

The auxetic material may be polymeric.

The liner may be in the form of a metallic, auxetic mesh structure.

The auxetic material may be of a porous nature.

The auxetic material forming the liner may comprise a biodegradable polymer or polymers. This may be advantageous in allowing breakdown of the stent in the body over the course of time.

An auxetic material for use in the invention may be selected from any suitable material, including the known auxetic materials mentioned below.

Synthetic auxetic materials are known from for example US Patent No. 4668557 which discloses preparation as an open-celled polymeric foam, negative Poisson ratio properties being secured by mechanical deformation of the foam by compression. Auxetic materials may also be in the form of microporous polymers, polymer gels, and macroscopic cellular structures (e.g. structures comprising re-entrant "bow tie"or inverted hexagon units). A polymeric material is disclosed in International Patent Application No. WO 91/01210, the material having an auxetic microstructure of fibrils connected at nodes and being obtained by compacting polymer particles at elevated temperatures and pressures, sintering and then deforming the compacted polymer by extrusion through a die to produce a cylindrical rod of auxetic material. International Patent Application No. WO 00/53830 discloses an auxetic polymeric material which is of filamentary or fibrous form which is produced by cohering and extruding thermoformable particulate material, cohesion and extrusion being effected with spinning so that an auxetic microstructure of fibrils and nodes can be obtained without requiring separate sintering and compaction stages. Auxetic materials have for example been produced of polytetrafluoroethylene, polyethylene, nylon and polypropylene.

A liner in accordance with the invention typically comprises an auxetic material produced by:

machining appropriate geometry, e.g. inverted microhexagons, into the structure; or

processing, i.e. compression and subsequent deformation of polymeric powder particles into a tubular form under controlled conditions of pressure and temperature; or

a combination of processing and subsequent micromachining.

Appropriate geometry such as inverted microhexagons can be machined into the material which forms or is to form the tubular liner using an excimer laser system. Machining by means of excimer laser technology allows feature sizes from about 4mm to about 2 micron to be etched into a wide variety of materials and features of the order of 10 micron in size or larger can be drilled through the entire thickness of a substrate.

The tubular liner may comprise a stent for insertion, e.g. with the aid of a catheter, into an *in vivo* duct, examples of which are given hereinbefore.

The tubular liner may be sufficiently flexible that, by virtue of the synclastic property of auxetic materials, it can be readily turned inside out within the confines of a duct, e.g. a blood vessel or other *in vivo* duct, in which it is to be installed or implanted.

According to a second aspect of the present invention there is provided a method of inserting a flexible tubular liner as defined above into a duct, said method comprising locating the tubular liner on a mandrel surrounded by a sleeve, passing the assembly of sleeve, liner and mandrel into the duct and effecting relative movement of the mandrel relative to the sleeve so that the tubular liner is displaced through the open end of the sleeve in such a way that it folds back over the sleeve and turns inside out within the

confines of the duct, and withdrawing the sleeve and mandrel from the duct to leave the liner in situ.

Also according to the present invention there is provided an assembly for use in lining a section of a duct, the assembly comprising a mandrel, a tubular liner of auxetic material carried by the mandrel and a sleeve surrounding the mandrel and the liner, the mandrel being movable relative to the sleeve.

The open end of the sleeve through which the liner is displaced may have a convexly curved end face to facilitate folding back of the liner over the sleeve.

The mandrel may be provided with a heating element for use, for example, in softening up and/or predilation of material deposited within the duct. Alternatively or additionally the mandrel may be provided with a laser radiation transmission path, e.g. a fibre optic, to allow laser radiation to be directed into the duct, for instance to treat clogged or plaque-filled ducts.

The mandrel may be provided with a passageway or passageways in communication with the leading end portion of the mandrel to allow fluids to be withdrawn from the duct.

The arrangement may be such that, during insertion of the liner, fluid flow (e.g. blood flow) through the assembly is possible. This may be achieved for instance by providing one or more apertures or slits in the sleeve as well as in the mandrel so that fluid flow can take place from one side of the assembly to the other via a pathway extending from said one side, around the outside of the assembly, through the apertures or slits in the sleeve and mandrel and to the other side of the assembly. For instance, in the case of a

stent, during insertion of the stent such an arrangement may allow blood flow from a point upstream of a narrowing or obstruction to a point downstream thereof.

The mandrel may include a portion which may be radially expanded. This may server to facilitate dilation of obstructions such as plaque in the duct, e.g. during deployment of the liner, and/or facilitate "back folding" of the leading part of the liner around the sleeve.

The liner may be adapted for use in the delivery of drugs or other beneficial agents, e.g to the site of narrowing or obstruction in an *in vivo* duct such as an artery. Fabrication of the liner from biodegradable materials may be advantageous in this context because of the possibility of exploiting biodegradability in terms of the release profile of such agents from the liner.

The invention will now be described by way of example only with reference to the accompanying drawings, in which:

Figure 1 illustrates the geometrical features of an auxetic material which may be made use of in a tubular liner or stent in accordance with the present invention;

Figures 2A to 2D illustrate the inversion of an auxetic tubular structure of relatively short length;

Figure 3 is a sectional view of an assembly for use in implanting a stent within an *in vivo* duct such as a blood vessel;

Figure 4 is an enlarged view showing details of the mandrel of the assembly shown in Figure 3;

Figures 5 to 7 are views showing successive stages in the use of the assembly to implant the stent within a blood vessel or the like;

Figure 8 and 9 are views illustrating transfer of the stent on to the mandrel during the course of preparing the assembly of Figure 3;

Figure 10 is a perspective view of a modified form of stent provided with incisions for allowing access to side branches of the duct in which the stent is to be implanted; and

Figure 11 is a plan view of the stent of Figure 10.

Referring to Figure 1, this illustrates a typical geometry (inverted hexagons 12 or bow tie honeycomb) which may be micromachined by for example excimer laser technology so as to impart auxetic properties to a substrate material. It will be seen that the application of a tensile load in direction A will result in expansion of the structure in direction B in contrast with conventional materials having a positive Poisson ratio. However, the present invention is not limited to securing auxetic properties by micromachining of geometrical features; such properties may be derived by other methods known in the art, e.g. compression and deformation of polymeric powder particles into a tubular structure under controlled temperature and pressure conditions to produce a material which is, in effect, intrinsically auxetic.

Consideration of the synclastic property of auxetic materials has led the present applicant to the recognition that a tubular liner, e.g. a stent for implantation in an

*in vivo* duct, may be readily inverted or turned inside out. This effect is illustrated in Figures 2A to 2D. Starting with a relatively short section of a tubular structure 10 having upper and lower ends 14, 16 (Figure 2A), the structure is compressed laterally, which for the purposes of illustration is supported by a surface underneath its lower surface 16. The structure may be manipulated by releasing the lower end 16, whose diameter as a result increases, while at the same time pressing the upper end 14 towards the support structure (Figure 2B). For example, this effect is possible if the structure 10 is based on the inverted microhexagon geometery of Figure 1 so arranged that the sides 11 of the hexagons are oriented in the circumferential direction with respect to the structure 10.

Assuming that the material forming the structure 10 is sufficiently flexible, such compression may be continued until the upper end 14 is drawn towards the plane containing the lower end 16 (see Figure 2C) thus allowing it to be passed through that plane so that, as shown in Figure 2D, the tubular structure is inverted or turned inside out and the upper end 14 becomes the lower end 16 and *vice versa*.

The above inversion effect is exploited in the present invention for the purpose of lining a duct, e.g. inserting a stent into an obstructed or narrowed in that the liner or stent employed is of an auxetic material and is sufficiently flexible that it may be inverted within the confines of the duct. For ease of reference, the invention will be described below in terms of a stent for implantation in a blood vessel but it is to be understood that the invention is not limited to this particular application.

Referring now to Figures 3 to 7, the stent 20 comprises a tubular structure of material which may be intrinsically auxetic or may have been rendered auxetic by suitable techniques such as micromachining of appropriate geometrical features. The stent 20 is located on a reduced diameter leading portion 22 of a mandrel 24 and is in a compressed state between the portion 22 and an outer sleeve 26. The mandrel 24 and the sleeve 26 are

arranged so as to be movable relative to one another and are typically made of a low friction/non-stick material such as polytetrafluoroethylene.

The tip 28 of the mandrel portion 22 is of tapering configuration and initially projects to some extent beyond the leading end of the sleeve 26. The assembly comprising the mandrel, stent and sleeve is, in use, coupled to a catheter device so that it can be introduced in the usual manner and positioned in the vicinity of an obstruction or narrowing of the blood vessel. The arrangement is such that the user may operate the assembly through the catheter device to effect movement of the mandrel 24 relative to the sleeve 26 as desired.

Initially or at some point during the procedure, the leading end of the stent 20 projects beyond the leading end of the sleeve 26 and by virtue of its auxetic properties tends to curl around that end in the manner illustrated in Figure 6. To facilitate this, the end face 29 of the sleeve 26 is convexly curved.

Once the assembly has been positioned close to the site of obstruction or narrowing of the duct 31 (see plaque deposits 30 in Figures 5 to 7) with the aid of a catheter, the mandrel 24 can be manipulated to move forwardly relative to the sleeve 26 so that the stent 20 is advanced forwardly also through its contact with shoulder 32 at the junction between mandrel portion 22 and the remainder of the mandrel. By progressive manipulative operations of the mandrel and sleeve, the stent 20 can be caused to begin inverting so that it folds back over the exterior of the sleeve 26. At the same time, as the stent passes out of the gap between the mandrel portion 22 and the sleeve 26, it is no longer subjected to compression and because of its auxetic properties, it can expand. In this manner, the stent can be transferred from the assembly into the blood vessel and expand and exert pressure on the plaque or deposit to reduce the obstruction or narrowing (see Figure 7). Eventually after the stent 20 has been fully deployed within the blood vessel, the

mandrel 24 and sleeve 26 may be withdrawn with the aid of the catheter leaving the stent *in situ*.

Upon self-expansion, the stent forms a region of relatively high curvature during the time that it is undergoing inversion. The resulting "travelling" curved front affords the potential for exerting a sufficiently high pressure to flatten any lesion or further flatten it after pre-dilation.

To facilitate pre-dilation of the duct and thereby assist lining up of the stent during deployment, the mandrel 24 may be designed so that, in the region of its leading end, it may be radially expanded. This can be implemented by providing the mandrel with a central rod 34 which extends through a longitudinal passageway in the mandrel and which has its leading end captive with the leading end of the mandrel portion 22. A section 38 of the portion 22 is formed with a cavity 36 (see Figure 4) and the walls of the portion 22 is provided with a number of longitudinal slits or apertures (not illustrated) so that this section 38 of the portion 22 can be caused to expand radially by pulling the rod 34 backwards in direction C relative to the mandrel. When the mandrel is displaced forwardly of the sleeve 26 so as to expose the slitted or apertured section 38, expansion of the section 38 can be effected by appropriate manipulation of the rod 34 and mandrel 24 and this can be used to pre-dilate the deposit or plaque 30 to some extent in the artery or duct. The rod 34 may, if desired, be a good heat conductor (e.g. a suitable metal) so that heating of the rod may be used to heat up the deposit or plaque 30 and soften the same and assist in pre-dilation. An alternative is to use a rod 34 in the form of a quartz optic fibre catheter through which radiation, e.g. near-ultraviolet radiation from an excimer laser, may be transmitted to the leading end of the mandrel to treat the deposit or plaque material obstructing the artery or the like.

Another feature that may be employed is to provide the mandrel with a longitudinal passageway through which fluidised material (e.g. created by heating or laser treatment of the deposit) can be withdrawn or through which blood flow can be facilitated during stent deployment. In the embodiment illustrated in Figure 4, this is implemented by using a hollow rod 34 having holes 40 at its distal end to allow fluid entry into the passageway within the rod. Some of the holes may be provided in registry with the cavity 36 so that fluidised material entering via the longitudinal slits or apertures of section 38 can be drawn into the interior of the hollow rod 34.

In a modification as illustrated in Figure 3 by phantom lines , the mandrel 24 may be telescopic with the portion 22 forming an inner section 22A telescopically received within an outer section 24A of the mandrel. so that the inner and outer mandrel sections can be displaced relative to one another when it is convenient to do so, e.g. during stent deployment or during fabrication of the assembly comprising the stent, mandrel and sleeve (as described below with reference to Figures 8 and 9). This arrangement may for instance be employed, in conjunction with the expansion feature described with reference to Figure 4, to facilitate backfolding of the initial part of the stent around the leading end of the sleeve 26.

In another modification, as discussed hereinbefore, a pathway or pathways may be provided for fluid flow from one end of the assembly to the other so that, for example, blood may flow through the assembly from a location upstream of the narrowing or obstruction in an artery to a location downstream thereof. The fluid flow pathway(s) may for instance be provided by the provision of strategically located apertures or slits in the sleeve 26 and the mandrel 22, 24.

Referring now to Figures 8 and 9, the production of the assembly comprising the compressed stent 20, the mandrel 24 and the sleeve 26 is illustrated. Initially the tube

20 of auxetic material is manufactured around a tubular former 50 which is assembled with the mandrel 24 and a housing 52. The housing 52 functions in extruder-like fashion and has an internal curved end face 54 acting as a guide for transfer of the auxetic tube from the former 50 onto the mandrel portion 22 . A plunger 55 is assembled to the former 50 (see Figure 8) and is advanced forwardly to displace the auxetic tube 20 and "extrude" it out of the gap between the former 50 and the housing 52 and onto the mandrel portion 22 (see Figure 9). At the same time, the mandrel 22 is displaced so that the tube 20 locates on to the mandrel section 22 with one end of the tube 20 immediately adjacent the shoulder 32. Once the tube 20 has been transferred to the mandrel, the housing 52 may be removed and the sleeve 26 is used to displace the former 50 by abutting the leading end of the sleeve 26 against the trailing end 58 of the former and moving the sleeve 26 forwardly to slide the former 50 over the auxetic tube 20 until the sleeve 26 is substituted for the former 50. In this way, the auxetic tube forming the stent 20 is located, in a compressed state, between the mandrel portion 22 and the sleeve 26.

Where desired, the stent may be adapted for use in situations in which there is a requirement for access to artery side branches over the stented section of a main artery. Referring to Figures 10 and 11, the stent 20 is provided with one or more side openings 60 which are located at different circumferential positions relative to an imaginary axial plane 70 depicted in Figure 10. Such openings may be produced during the production of the assembly as described in relation to Figures 8 and 9, i.e. by using a suitable template to form the openings in the stent while it is located on the former 50. The openings may be in the form of holes or, as shown in Figures 10 and 11, they may be created by slits or incisions in the wall of the stent, e.g. each opening 60 being formed by a combination of a longitudinal slit 62 and a circumferential slit 64.

The stent may, if desired, be used as a vehicle for delivery of drugs or other beneficial agents to the site of the narrowing or obstruction, e.g. wound-healing agents or

DNA materials such as oligopeptides. Such agents may be incorporated in the porous auxetic material, e.g. by chemical and/or physical fixation. The drug or other agent can be incorporated into the interstitial voids or it can be introduced by blending into polymeric particles which are to be used in production of the stent, either by processing into a microporous auxetic tube or into a non-auxetic tube which is subsequently transformed into an auxetic scaffolding, e.g. by micromachining.

It is envisaged that the double curvature property of auxetic materials will confer advantages relative to conventional metal stents in that stent removal by mechanical manipulation may be facilitated without damaging the surrounding artery. This two-way flexibility of auxetic materials may also assist in avoiding the formation of blood clots and/or overgrowth of scar tissue due to "self-correction" as discussed, in relation to filters, in International Patent Application No. WO 99/22838 at Page 12, line 29 to Page 13, line 14.

Although the possibility of the stent being metallic is not excluded, production of the stent using a polymer of suitable tissue-compatibility is preferred since it eliminates the risk, which can occur where metallic stents are deployed, of chemical reaction between the metal and its immediate environment (i.e. dilated plaque tissue).

Whilst endeavouring in the foregoing specification to draw attention to those features of the invention believed to be of particular importance, it should be understood that the Applicant claims protection in respect of any patentable feature or combination of features disclosed herein and/or shown in the drawings whether or not particular emphasis has been placed on such feature or features.

Fig 1

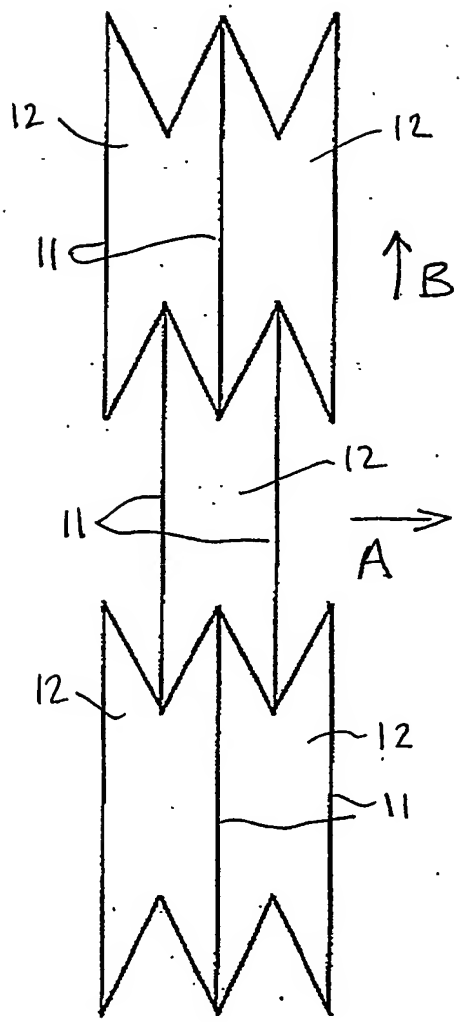



Fig 2A

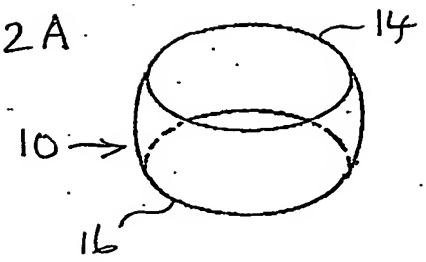



Fig 2B

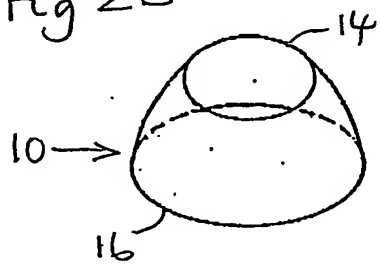



Fig 2C

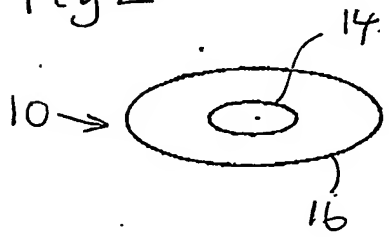
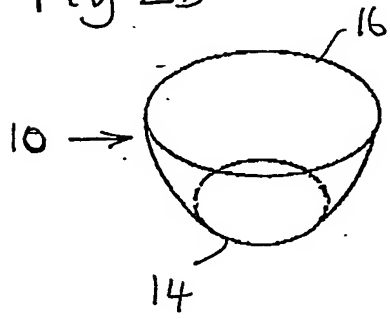



Fig 2D



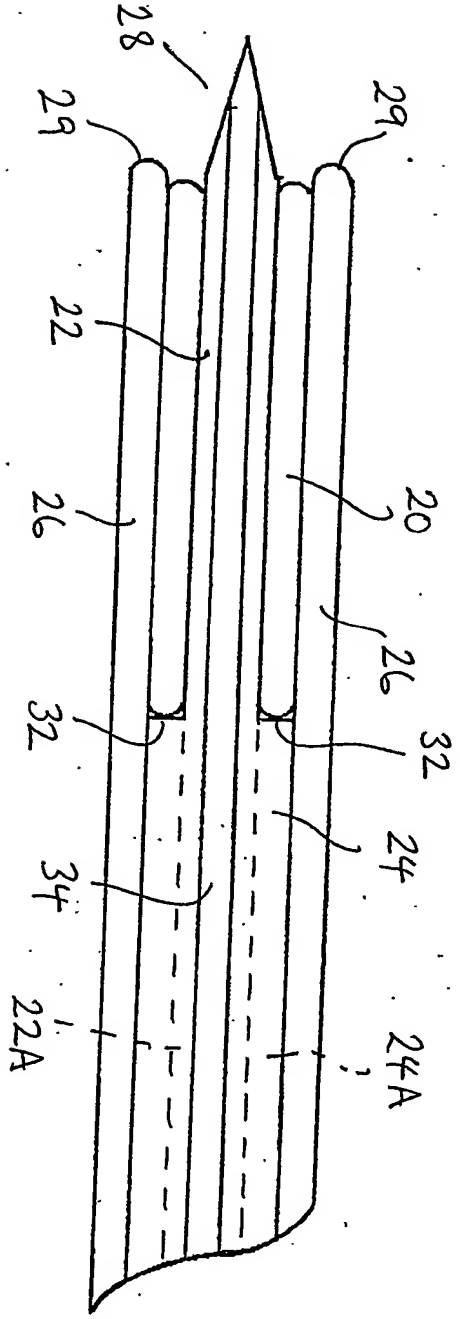



Fig 3

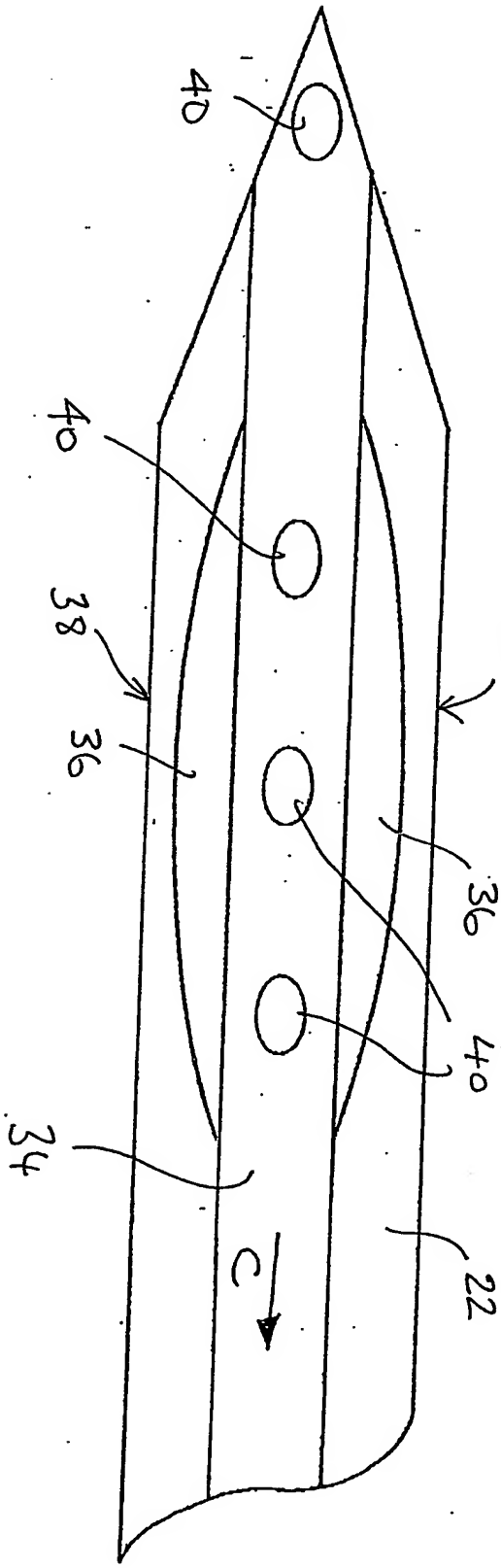



Fig 4

Fig 5

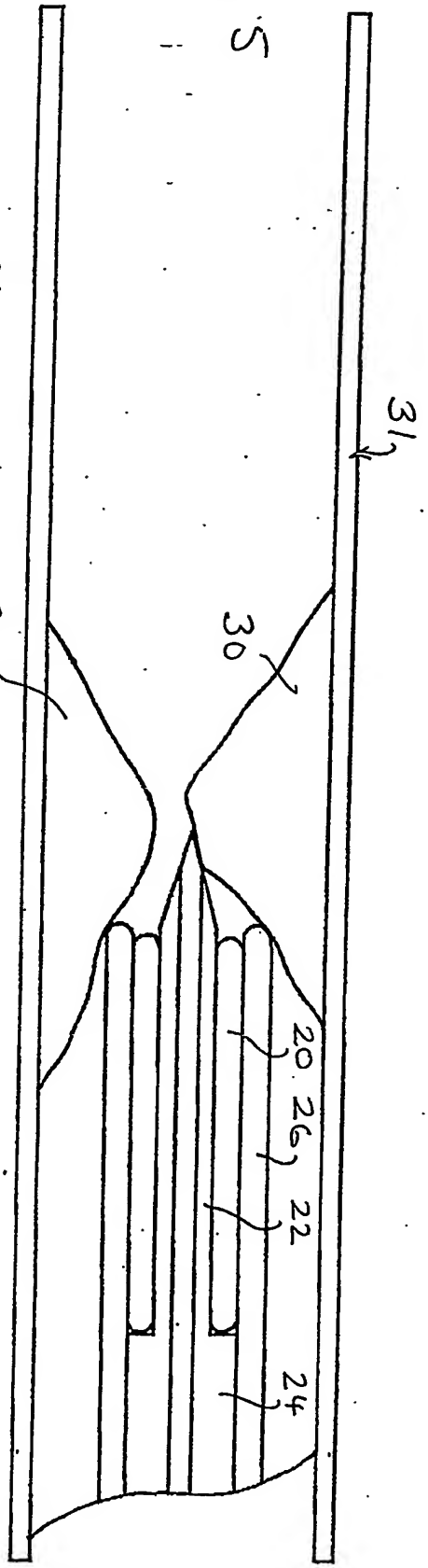



Fig 6

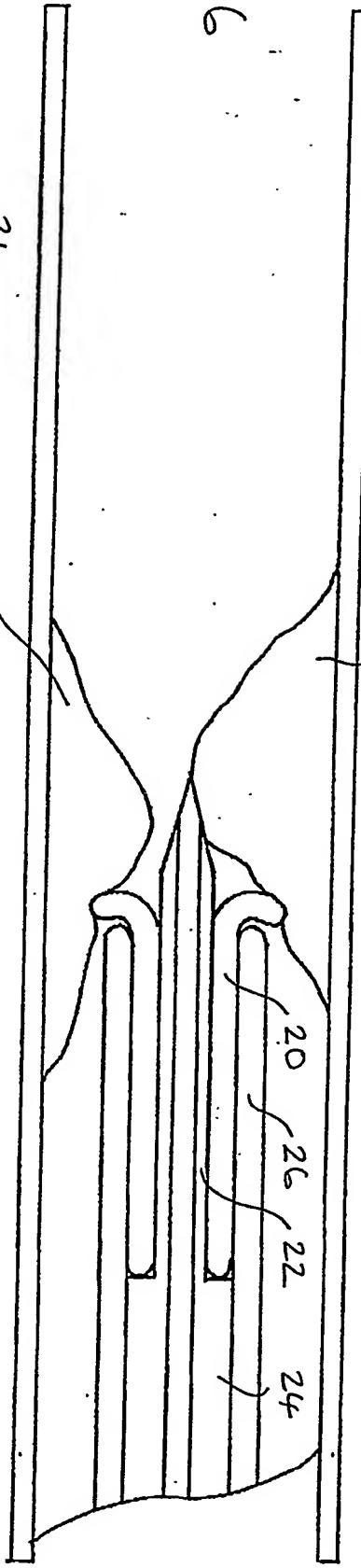



Fig 7

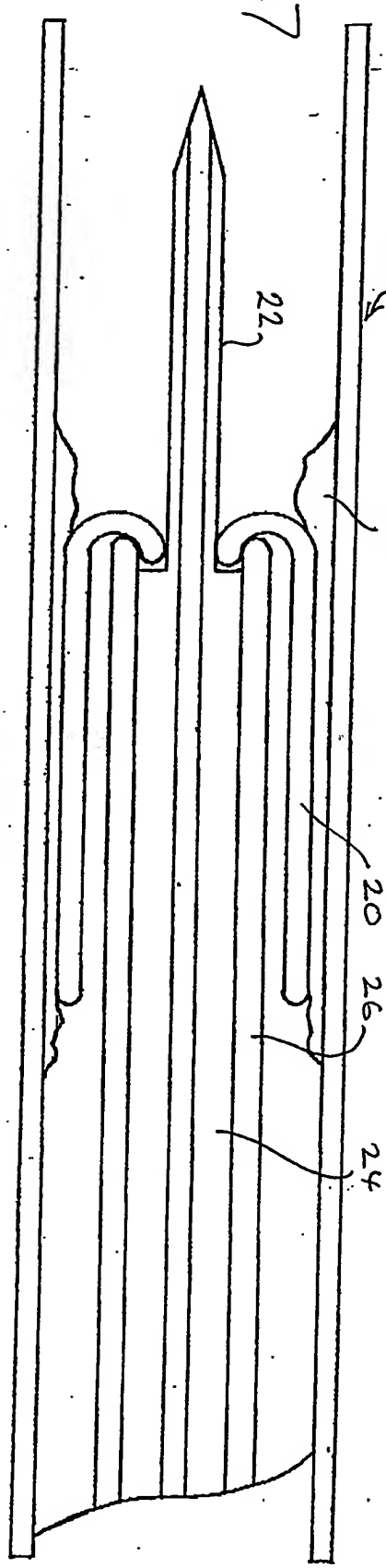


Fig 8

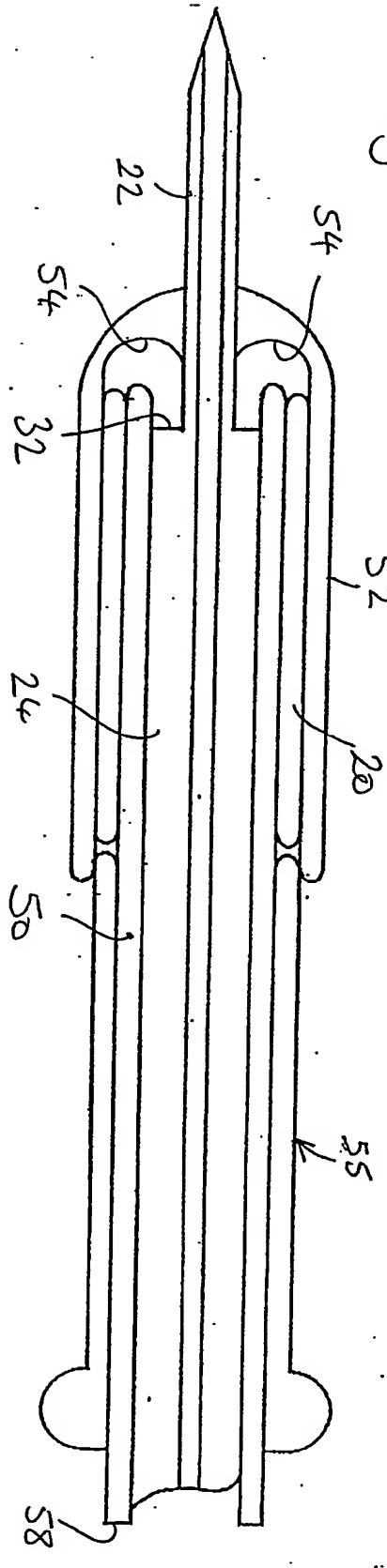
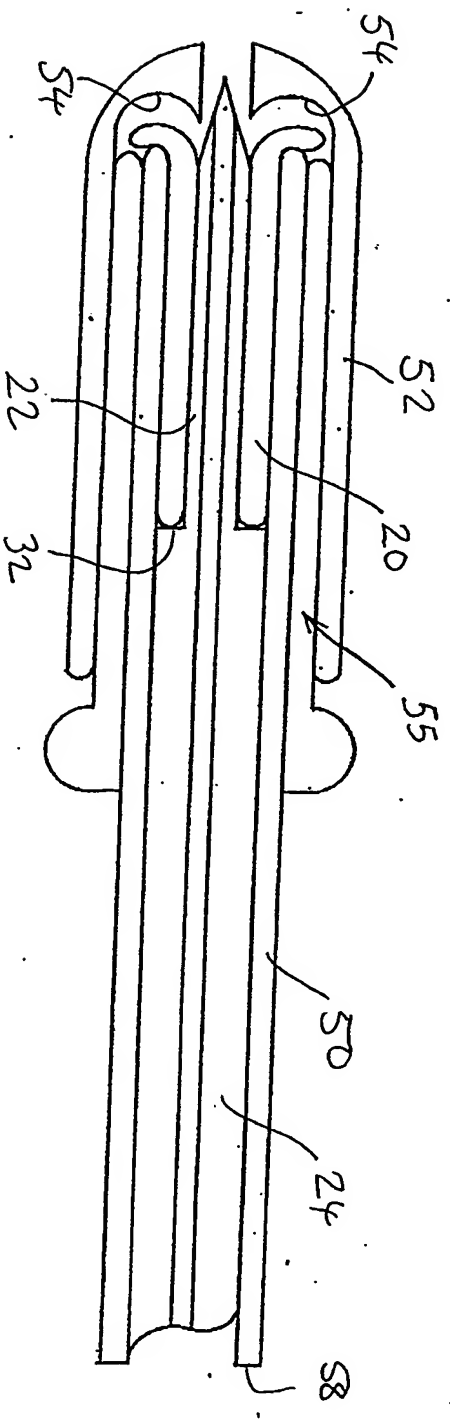



Fig 9



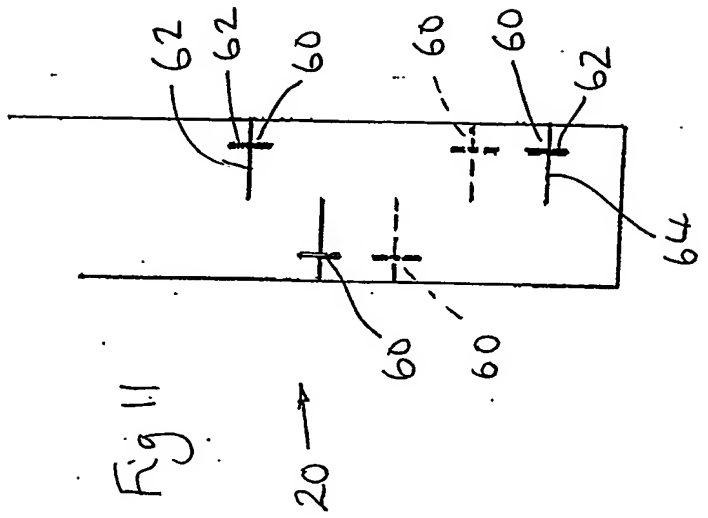



Fig 11

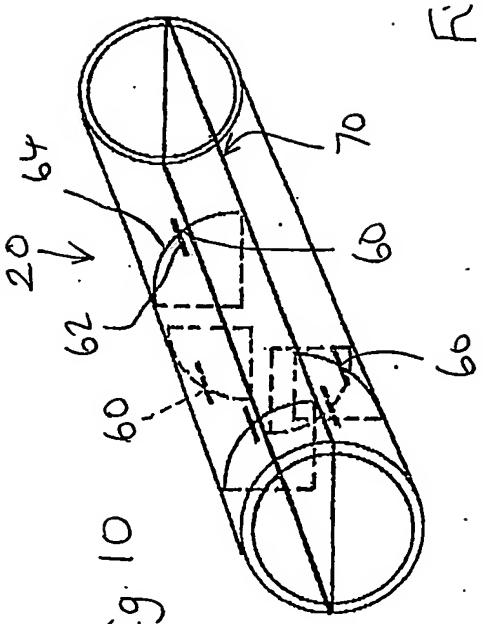



Fig 10

PCT Application

GB0303393